

REC'D 16 JUL 2004
WIPO PCT/SG2004/000202

**REGISTRY OF PATENTS
SINGAPORE**

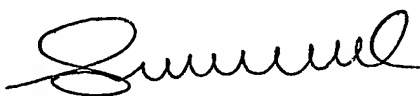
This is to certify that the annexed is a true copy of following application as filed with the Registry.

Date of Filing : 07 JUL 2003

Application Number : 200304160-5

Applicant(s) /
Proprietor(s) of Patent : AGENCY FOR SCIENCE, TECHNOLOGY
AND RESEARCH

Title of Invention : METHOD AND APPARATUS FOR
EXTRACTING THIRD VENTRICLE
INFORMATION


Sandra Lynn Merinda (Ms)
Assistant Registrar
for REGISTRAR OF PATENTS
SINGAPORE

08 Jul 2004

**PRIORITY
DOCUMENT**
SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH RULE 17.1(a) OR (b)

Best Available Copy

INTELLECTUAL PROPERTY OFFICE OF SINGAPORE
REQUEST FOR THE GRANT OF A PATENT UNDER
SECTION 25

101101

* denotes mandatory fields

1. YOUR REFERENCE*

SP5634

2. TITLE OF
INVENTION*

METHOD AND APPARATUS FOR EXTRACTING THIRD VENTRICLE
INFORMATION

3. DETAILS OF APPLICANT(S)* (see note 3)

Number of applicant(s)

1

(A) Name

Agency for Science, Technology and Research

Address

10 Science Park Road, #01-01/03 The Alpha,
Singapore 117684

State

Country

SG

☒

For corporate applicant

☐

For individual applicant

State of incorporation

State of residency

Country of incorporation

SG

Country of residency

☐

For others (please specify in the box provided below)

(B) Name

Address

State

Country



☐

For corporate applicant

☐

For individual applicant

State of incorporation

State of residency

Country of incorporation

Country of residency

☐

For others (please specify in the box provided below)

(C) Name

Address

State

Country

☐

For corporate applicant

☐

For individual applicant

State of incorporation

State of residency

Country of incorporation

Country of residency

☐

For others (please specify in the box provided below)

☐

Further applicants are to be indicated on continuation sheet 1

4. DECLARATION OF PRIORITY (see note 5)

A. Country/country designated

File number

Filing Date

DD MM YYYY

B. Country/country designated

File number

Filing Date

DD MM YYYY

☐

Further details are to be indicated on continuation sheet 6

5. INVENTOR(S)* (see note 6)

A. The applicant(s) is/are the sole/joint inventor(s)

Yes

☐

No

☒

B. A statement on Patents Form 8 is/will be furnished Yes ☒ No ☐

6. CLAIMING AN EARLIER FILING DATE UNDER (see note 7)

☐ section 20(3) ☐ section 26(6) ☐ section 47(4)

Patent application number

DD MM YYYY

Filing Date

Please mark with a cross in the relevant checkbox provided below
(Note: Only one checkbox may be crossed.)

☐ Proceedings under rule 27(1)(a)

DD MM YYYY

Date on which the earlier application was amended

☐ Proceedings under rule 27(1)(b)

7. SECTION 14(4)(C) REQUIREMENTS (see note 8)

Invention has been displayed at an international exhibition. Yes ☐ No ☒

8. SECTION 114 REQUIREMENTS (see note 9)

The invention relates to and/or used a micro-organism deposited for the purposes of disclosure in accordance with section 114 with a depositary authority under the Budapest Treaty.

Yes ☐ No ☒

9. CHECKLIST*

(A) The application consists of the following number of sheets

i.	Request	<input type="text" value="5"/>	Sheets
ii.	Description	<input type="text" value="14"/>	Sheets
iii.	Claim(s)	<input type="text" value="4"/>	Sheets
iv.	Drawing(s)	<input type="text" value="1"/>	Sheets
v.	Abstract (Note: The figure of the drawing, if any, should accompany the abstract)	<input type="text" value="1"/>	Sheets
Total number of sheets		<input type="text" value="25"/>	Sheets

(B) The application as filed is accompanied by:

☐ Priority document(s) ☐ Translation of priority document(s)



Statement of Invention
& right to grant



International exhibition certificate

10. DETAILS OF AGENT (see notes 10, 11 and 12)

Name

Firm

LLOYD WISE

11. ADDRESS FOR SERVICE IN SINGAPORE* (see note 10)

Block/Hse No.

Level No.

Unit No./PO Box

Street Name

P.O BOX 636

Building Name

TANJONG PAGAR POST OFFICE

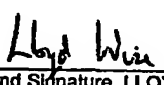
Postal Code

910816

12. NAME, SIGNATURE AND DECLARATION (WHERE APPROPRIATE) OF APPLICANT OR AGENT* (see note 12)
(Note: Please cross the box below where appropriate.)

☒ X

I, the undersigned, do hereby declare that I have been duly authorised to act as representative, for the purposes of this application, on behalf of the applicant(s) named in paragraph 3 herein.


Name and Signature LLOYD WISE

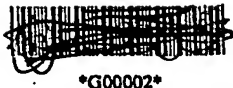
DD MM YYYY

07 07 2003

Our Ref SP5634

NOTES:

1. This form when completed, should be brought or sent to the Registry of Patents together with the rest of the application. Please note that the filing fee should be furnished within the period prescribed.
2. The relevant checkboxes as indicated in bold should be marked with a cross where applicable.
3. Enter the name and address of each applicant in the spaces provided in paragraph 3.
Where the applicant is an individual
 - Names of individuals should be indicated in full and the surname or family name should be underlined.
 - The address of each individual should also be furnished in the space provided.
 - The checkbox for "For individual applicant" should be marked with a cross.
 Where the applicant is a body corporate
 - Bodies corporate should be designated by their corporate name and country of incorporation and, where appropriate, the state of incorporation within that country should be entered where provided.
 - The address of the body corporate should also be furnished in the space provided.
 - The checkbox for "For corporate applicant" should be marked with a cross.
 Where the applicant is a partnership
 - The details of all partners must be provided. The name of each partner should be indicated in full and the surname or family name should be underlined.
 - The address of each partner should also be furnished in the space provided.
 - The checkbox for "For others" should be marked with a cross and the name and address of the partnership should be indicated in the box provided.
4. In the field for "Country", please refer to the standard list of country codes made available by the Registry of Patents and enter the country code corresponding to the country in question.
5. The declaration of priority in paragraph 4 should state the date of the previous filing, the country in which it was made, and indicate the file number, if available. Where the application relied upon in an International Application or a regional patent application e.g. European patent application, one of the countries designated in that application (being one falling under section 17 of the Patents Act) should be identified and the country should be entered in the space provided.
6. Where the applicant or applicants is/are the sole inventor or the joint inventors, paragraph 5 should be completed by marking with a cross the 'YES' checkbox in the declaration (A) and the 'NO' checkbox in the alternative statement (B). Where this is not the case, the 'NO' checkbox in declaration (A) should be marked with a cross and a statement will be required to be filed on Patents Form 8.
7. When an application is made by virtue of section 20(3), 26(6) or 47(4), the appropriate section should be identified in paragraph 6 and the number of the earlier application or any patent granted thereon identified. Applicants proceeding under section 26(6) should identify which provision in rule 27 they are proceeding under. If the applicants are proceeding under rule 27(1)(a), they should also indicate the date on which the earlier application was amended.
8. Where the applicant wishes an earlier disclosure of the invention by him at an International Exhibition to be disregarded in accordance with section 14(4)(c), then the 'YES' checkbox at paragraph 7 should be marked with a cross. Otherwise, the 'NO' checkbox should be marked with a cross.
9. Where in disclosing the invention the application refers to one or more micro-organisms deposited with a depository authority under the Budapest Treaty, then the 'YES' checkbox at paragraph 8 should be marked with a cross. Otherwise, the 'NO' checkbox should be marked with a cross. Attention is also drawn to the Fourth Schedule of the Patents Rules.
10. Where an agent is appointed, the fields for "DETAILS OF AGENT" and "ADDRESS FOR SERVICE IN SINGAPORE" should be completed and they should be the same as those found in the corresponding Patents Form 41. In the event where no agent is appointed, the field for "ADDRESS FOR SERVICE IN SINGAPORE" should be completed, leaving the field for "DETAILS OF AGENT" blank.
11. In the event where an individual is appointed as an agent, the sub-field "Name" under "DETAILS OF AGENT" must be completed by entering the full name of the individual. The sub-field "Firm" may be left blank. In the event where a partnership/body corporate is appointed as an agent, the sub-field "Firm" under "DETAILS OF AGENT" must be completed by entering the name of the partnership/body corporate. The sub-field "Name" may be left blank.
12. Attention is drawn to sections 104 and 105 of the Patents Act, rules 90 and 105 of the Patents Rules, and the Patents (Patent Agents) Rules 2001.
13. Applicants resident in Singapore are reminded that if the Registry of Patents considers that an application contains information the publication of which might be prejudicial to the defence of Singapore or the safety of the public, it may prohibit or restrict its publication or communication. Any person resident in Singapore and wishing to apply for patent protection in other countries must first obtain permission from the Singapore Registry of Patents unless they have already applied for a patent for the same invention in Singapore. In the latter case, no application should be made overseas until at least 2 months after the application has been filed in Singapore, and unless no directions had been issued under section 33 by the Registrar or such directions have been revoked. Attention is drawn to sections 33 and 34 of the Patents Act.
14. If the space provided in the patents form is not enough, the additional information should be entered in the relevant continuation sheet. Please note that the continuation sheets need not be filed with the Registry of Patents if they are not used.



G00002

Method And Apparatus For Extracting Third Ventricle Information

Field of the Invention

The present invention is directed to a method and apparatus for extracting third ventricle information of a brain from images thereof.

Background of the Invention



150150

Magnetic Resonance Imaging (MRI) can be used in diagnosis of various diseases in humans. The most important property to be considered in MRI is the stimulation of the tissue with various radio-frequency (RF) pulses at definite time intervals and then to detect the resultant echoes. The precise timing of the RF pulses is vitally important for good imaging. The RF pulses can be repeated at a certain rate (TR) and the echoes can be detected at a certain time (TE). The relative time lengths of TR and TE determine the pulse sequences and hence the tissue visualization.

The spin echo pulse sequence is the most commonly used pulse sequence. The pulse sequence timing can be adjusted to give T1-weighted, Proton or spin density, and T2-weighted images. The two variables of interest in spin echo sequences are the TR and TE. All spin echo sequences include a slice selective 90 degree pulse followed by one or more 180 degree refocusing pulses.

A short TR and short TE will give a T1-weighted image, a long TR and short TE will give a proton density image, and a long TR and long TE will give a T2-weighted image.

Fluid attenuated inversion recovery (FLAIR) is a type of inversion recovery sequence to give heavy T1-weighting. The basic part of an inversion recovery sequence is a 180 degree RF pulse that inverts the magnetization followed by

a 90 degree RF pulse that brings the residual longitudinal magnetization into the x-y or transverse plane where it can be detected by an RF coil. The time between the initial 180 degree pulse and the 90 degree pulse is the inversion time (TI).

The spoiled gradient echo recovery (SPGR) sequence has the same TE and TR as T1-weighted sequence but has an additional variable flip/tip angle of the spins. The flip angle is usually at or close to 90 degrees for a spin echo sequence but commonly varies over a range of about 10 to 80 degrees with gradient echo sequences. The larger tip angles give more T1 weighting to the image and the smaller tip angle give more T2 or actually T2* weighting to the images.

The size and morphology of the third ventricle is important in clinical pathology. As the third ventricle is situated in a very critical part deep inside the brain, any lesion in the surrounding tissues would affect its shape and orientation. Mass lesion in the brain would cause mass effect and directly influence the orientation of the third ventricle.

Early intracerebral haemorrhage is difficult to visualise on CT images. The orientation of the third ventricle is key in its identification. As there is mass effect on one side, the third ventricle would shift from its midline position and its long axis would also change with respect to the symmetry plane of the skull. An efficient way to extract the third ventricle plane would facilitate the identification of the early intracerebral haemorrhage and localisation of the two landmarks, namely the anterior commissure AC and posterior commissure PC, for spatial normalisation of the human brain.

The size and width of the third ventricle are also important clinical parameters. The third ventricle may be enlarged in either generalised or localised hydrocephalus. The usual cause is blockage of the aqueduct of Sylvius¹. Patients with Alzheimer's disease², bipolar disorders³ and manic depression⁴ have wider third ventricles. The width of the third ventricle better reflects the degree of cholinergic deficit than the severity of histopathological changes, such as scores of plaques and tangles in the brain of a patient with Alzheimer Disease⁵.

Existing methods for identifying the above-mentioned pathology conventionally use ventricle segmentation.

US 6 434 030 describes an automated method and/or system for identifying suspected lesions in a brain based on the application of a segmentation technique to at least one of the masked images to classify the varying pixel intensities and differentiate hyper-intense regions.

US 6 205 235 illustrates a method for non-invasive imaging of an anatomic tissue structure in isolation from surrounding tissues based on live-wire segmentation and boundary definition.

US 6 208 347 describes a semi-automated method of MRI analysis based on mathematical modelling of MRI pixel intensity histograms.

WO 94/14132 describes a non-invasive scanning medical apparatus for generating an image of at least an interior region of a subject to be examined. The correlation of previous data to the scanned image is determined.

Methods which utilise segmentation techniques can run into problems and/or fail when there is a serious inhomogeneity and/or noise as such systems are

highly vulnerable to noise, inhomogeneity and various artefacts such as pathology (which causes the loss of anatomical information).

The present invention aims to substantially overcome or ameliorate the above-mentioned problems and the measurement of the width of the third ventricle will facilitate the identification of pathology.

The method according to the present invention allows the anatomical knowledge to be implicitly incorporated in the intelligent sampling scheme.

The method finds application in medical imaging, in particular neuroimaging and provides ways for quantifying anatomical structures. Other areas of applications include neuroinformatics, neurosurgery, neuroradiology and brain research.

Summary of the Invention

The invention is directed to a method and apparatus for quantifying the third ventricle without segmentation and specifically, the extraction of the third ventricular plane and calculation of the width of the third ventricle of the human or animal brain in neuroimages through intelligent sampling of anatomical structures around the third ventricle.

According to a first aspect of the present invention there is provided a method for extracting third ventricle information from images of a plurality of axial slices of a third ventricle of a brain having an anterior commissure and a posterior commissure, the third ventricle having a third ventricle plane and a width, the method comprising:

- a. determining a third ventricle midline for each of a number of the axial slices;
- b. determining the orientation of each of the midlines;
- c. generating a histogram of the orientations of the midlines;
- d. determining the peak of the histogram to provide a peak orientation;
- e. selecting the midlines having an orientation within a predetermined angle from the peak orientation; and
- f. calculating the third ventricle plane from the midlines having an orientation within the predetermined angle from the peak orientation.

Preferably, the step of calculating the third ventricle plane comprises calculating the least square fit plane of the midlines having an orientation within the predetermined angle from the peak orientation.

In a preferred embodiment, the step of calculating the third ventricle plane further comprises:

- (i) calculating the maximum distance from the least square fit plane to the midlines having an orientation within the predetermined angle from the peak orientation,
- (ii) generating a histogram of the maximum distance of the midlines having an orientation within the predetermined angle from the peak orientation to the least square fit plane,
- (iii) determining the peak of the histogram of the maximum distance of the midlines to the least square fit plane,
- (iv) selecting the midlines lying within a predetermined distance of the peak, and
- (v) recalculating the least square fit plane using the selected midlines to generate the third ventricle plane.

Preferably, the method further comprises calculating the width of the third ventricle, by for example, determining the axial slice having the anterior commissure and the posterior commissure, determining two lines parallel to the third ventricle plane in said determined slice, said two lines being tangential to the image of the third ventricle in said slice to indicate the boundary between the third ventricle and grey matter, and calculating the distance between the two parallel lines, said distance being representative of the width of the third ventricle.

Preferably, the step of determining the third ventricle midline for each of a number of the axial slice s_i comprises calculating the local symmetry index of a searching line segment, the third ventricle midline being the searching line segment that has the minimum local symmetry index.

The local symmetry index $lsl(x, y, s_i, \theta)$ may be calculated according to the following:

$$|ls(x, y, s_i, \theta)| \times lsl(x, y, s_i, \theta) = \sum_{(x_s, y_s)} \sum_k \text{DifG}(x_s, y_s, s_i, k)$$

where:

$|ls(x, y, s_i, \theta)|$ is the length of the searching line segment,

$ls(x, y, s_i, \theta)$ is the searching line segment of voxel (x, y, s_i) with the searching angle θ , and (x, y, s_i) the searching point,

$\cos(90^\circ + \theta)$ is denoted as $c90\theta$,

$\sin(90^\circ + \theta)$ is denoted as $s90\theta$,

$\text{fabs}(g(x_s + k \times c90\theta, y_s + k \times s90\theta, s_i) - g(x_s - k \times c90\theta, y_s - k \times s90\theta, s_i))$ is denoted as $\text{DifG}(x_s, y_s, s_i, k)$, where fabs is the absolute value function, the contribution of voxel (x_s, y_s, s_i) to $\text{Isi}(x, y, s_i, \theta)$ being:

$$\text{DifG}(x_s, y_s, s_i, 0.5) + \text{DifG}(x_s, y_s, s_i, 1.0) + \text{DifG}(x_s, y_s, s_i, 3.0) + \text{DifG}(x_s, y_s, s_i, 5.0) + \text{DifG}(x_s, y_s, s_i, 7.0).$$

In a preferred embodiment, the step of determining the axial slice having the anterior commissure and the posterior commissure comprises:

- (1) calculating the x co-ordinate of the voxel x_i for all of the axial slices where the third ventricle is present such that this voxel's y co-ordinate is the mass centre of s_i y_c , and (x_i, y_c, s_i) is on the third ventricle plane, that is $x_i = -(d + c s_i + b y_c)/a$, where (a, b, c) is a unit normal vector and d is a non-positive constant;
- (2) generating the searching line segment from (x_i, y_c, s_i) such that the line segment is on the third ventricle plane and its centre is (x_i, y_c, s_i) ;
- (3) calculating the average grey level avg_i of the searching line segment;
- (4) comparing the average grey level avg_i for different axial slices s_i and determining the axial slice having the anterior commissure and the posterior commissure.

Preferably, the step of determining the axial slice having the anterior commissure and the posterior commissure comprises for T1-, PD-weighted, FLAIR, and SPGR MR datasets, determining the axial slice with minimum average grey level avg_i , and for T2-weighted MR datasets it preferably comprises determining the axial slice with maximum average grey level avg_i .

According to a second aspect of the invention there is provided apparatus arranged to perform a method for extracting third ventricle information from images defined above.

According to a third aspect of the invention there is provided a computer program product comprising computer program instructions readable by a computer apparatus to cause the computer apparatus to perform a method defined above.

Brief Description of the Drawings

The present invention will now be described with reference to the sole figure, Figure 1, which is a flow diagram illustrating the steps involved in an algorithm according to an embodiment of the present invention.

Description of Preferred Embodiments

The steps constituting a preferred embodiment of the method of the present invention are shown in the flow diagram of Figure 1. The method of the present invention, will be discussed in more detail after a brief discussion of these steps.

Given the radiological images of the brain under consideration and the starting and ending axial slice (s_0 and s_n) where the third ventricle is present the processing steps illustrated in the flow diagram of Figure 1 are as follows:

Step 1 – extract the third ventricle midline segments for all of the axial slices in between the starting and ending axial slices s_0 and s_n inclusive;

Step 2 – remove outliers of the extracted midline segments;

Step 3 – calculate the third ventricle plane (PV3) from the extracted third ventricle midline segment inliers;

Step 4 – find the axial slice (APC) in between the starting and ending axial slices s_0 and s_n where the anterior commissure (AC) and posterior commissure (PC) are present; and

Step 5 – in the aforementioned axial slice (APC) locate the two line segments parallel to the third ventricle plane (PV3) and tangential to the third ventricle, the distance between them is taken as the width of the third ventricle.

A brain dataset or volume is represented as a stack of parallel two-dimensional slices. The three dimensional volume is denoted as $Vol(x,y,z)$ with x , y and z being the co-ordinates at voxel (x,y,z) . In this case, x , y and z are non-negative integers satisfying $0 \leq x \leq Xsize, 0 \leq y \leq Ysize, 0 \leq z \leq Zsize$ where the z co-ordinate is constant on the axial slices, the y co-ordinate is constant on the coronal slices and the x co-ordinate is constant on the sagittal slices.

If the original scanning orientation is coronal or sagittal, the axial slices are obtained by reorienting the original volume by reordering its voxels. The algorithm of the present invention works on the axial slices. The beginning and ending axial slices s_0 and s_n where the third ventricle is present are predetermined. Any axial slice in between s_0 and s_n is denoted as s_i , where s_i itself represents the axial slice as well as the axial slice number. The grey level at voxel (x,y,s_i) is denoted as $g(x,y,s_i)$. From voxel (x,y,s_i) numerous line segments can be drawn within s_i . The line segment is denoted as $ls(x,y,s_i,\theta)$ taking (x,y,s_i) as its centre, with the length of line segment being a constant L (for example, 60 mm) and the angle with respect to the y axis being θ . $ls(x,y,s_i,\theta)$ is called the searching line segment of voxel (x,y,s_i) with the searching angle θ , and (x,y,s_i) is called the searching point.

Step 1: Extract the third ventricle midline segments

A prominent feature of the third ventricle in axial slices is that the thalamus (grey matter, GM) and the third ventricle (cerebrospinal fluid, CSF) are substantially symmetrical with respect to the third ventricle midline. On axial slices, the length of the third ventricle may be up to 40 mm and its width may vary between around 3 mm to 10 mm. The centre of the third ventricle is around the mass centre of the axial slice.

To locate the third ventricle midline in an axial slice s_i , the local symmetry index of a searching line segment is used to capture the anatomical features of the third ventricle midline segment and thus to locate the third ventricle midline. Due to the variations in size of third ventricles, the local symmetry index should sample both the grey matter (GM) and cerebrospinal fluid (CSF).

For the searching line segment $l_s(x, y, s_i, \theta)$, its local symmetry index $l_{si}(x, y, s_i, \theta)$ measures the grey level symmetry around it. For each voxel (x_s, y_s, s_i) on the searching line segment, five pairs of sampling points at the opposite sides of $l_s(x, y, s_i, \theta)$ are taken on the lines perpendicular to $l_s(x, y, s_i, \theta)$ and passing through (x_s, y_s, s_i) with the distance to $l_s(x, y, s_i, \theta)$ preferably being 0.5 mm, 1 mm, 3 mm, 5 mm and 7 mm respectively.

$\cos(90^\circ + \theta)$ is denoted as $c90\theta$

$\sin(90^\circ + \theta)$ is denoted as $s90\theta$

$\text{fabs}(g(x_s + k \times c90\theta, y_s + k \times s90\theta, s_i) - g(x_s - k \times c90\theta, y_s - k \times s90\theta, s_i))$ is denoted as $\text{DifG}(x_s, y_s, s_i, k)$

The contribution of voxel (x_s, y_s, s_i) to $l_{si}(x, y, s_i, \theta)$ is:

$$\text{DifG}(x_s, y_s, s_i, 0.5) + \text{DifG}(x_s, y_s, s_i, 1.0) + \text{DifG}(x_s, y_s, s_i, 3.0) + \text{DifG}(x_s, y_s, s_i, 5.0) + \text{DifG}(x_s, y_s, s_i, 7.0)$$

where $\text{fabs}()$ is the absolute value function.

$\text{lsi}(x, y, s_i, \theta)$ is the average contribution of all the voxels on $\text{ls}(x, y, s_i, \theta)$, that is,

$$|\text{ls}(x, y, s_i, \theta)| \times \text{lsi}(x, y, s_i, \theta) = \sum_{(x_s, y_s) \in k} \text{DiffG}(x_s, y_s, s_i, k)$$

where $|\text{ls}(x, y, s_i, \theta)|$ is the length of the searching line segment in millimeters (mm).

The third ventricle midline segment on axial slice s_i is the searching line segment that has the minimum local symmetry index. The extracted third ventricle midline segment is called the approximated third ventricle midline segment (ATVMS).

Step 2: Remove outliers of the extracted midline segments

The approximated third ventricle midline segments (ATVMSs) are processed in two steps, to remove outliers, in the manner described for example in the applicants copending International Patent Application PCT/SG02/00231, the content of which is incorporated herein by way of reference.

Firstly, the orientations of all the ATVMSs are calculated and a histogram of the orientations is obtained. The peak of the histogram is determined and is called the peak orientation. Those ATVMSs with an orientation deviating from the peak orientation by more than a predetermined value, for example 1° , are considered as orientation 'outliers' while the rest of the ATVMSs are considered to be orientation 'inliers'.

Secondly, the least square fit plane of the orientation inliers is calculated. The maximum distance of all the orientation inliers to this plane is calculated and the peak of the histogram of all the distances is obtained. Those

orientation inliers with a distance deviating from the peak distance by more than a value of, for example 1mm, are considered the third ventricle plane outliers, while the rest of the orientation inliers are considered as the third ventricle inliers.

Step 3: Calculate the third ventricle plane

The third ventricle plane is approximated from the third ventricle inliers using, for example, the least square fit plane of the third ventricle inliers. The third ventricle plane is denoted as:

$$ax + by + cz + d = 0$$

where (a, b, c) is a unit normal vector and d is a non-positive constant.

Step 4: Find the axial slice with the anterior and posterior commissures

Any method for Identification of the anterior commissure (AC) and posterior commissure (PC) may be used to locate the axial slice with the two commissures thereon (APC). This may also be identified in the following way:

1. Calculate the x co-ordinate of the voxel x_i for all of the axial slices s_i in between the beginning and ending axial slices s_0 and s_n where the third ventricle is present such that this voxel and the mass centre of s_i have the same y coordinate y_c , and (x_i, y_c, s_i) is on the third ventricle plane, that is $x_i = -(d + c s_i + b y_c)/a$.
2. Form the searching line segment from (x_i, y_c, s_i) such that the line segment is on the third ventricle plane and its centre is (x_i, y_c, s_i) .
3. Calculate the average grey level of the searching line segment. For the axial slice s_i , the calculated average grey level is denoted as avg_i .
4. Compare the average grey level avg_i for different axial slices s_i . For T1-, PD-weighted, FLAIR, and SPGR MR datasets, the axial slice with minimum avg_i is taken as APC. For T2-weighted MR datasets, the axial slice with maximum avg_i is taken as APC.

5. Calculate the third ventricle width by locating the left-most and right-most lines parallel to the third ventricle plane and tangential to the third ventricle in the APC, that is the boundary between the third ventricle and the grey matter. The distance between the two parallel lines is defined as the third ventricle width.

In summary, the present invention is directed to a method of extracting the third ventricle plane which is robust to noise, inhomogeneity and various artefacts. It is also directed to calculating the width of the third ventricle of a brain from neuro images.

Extracting the third ventricle plane and measuring the width of the third ventricle is of clinical importance for both pathology detection and morphological description of brains. The present invention proposes a fast and automatic method for quantifying the third ventricle based on intelligent sampling of anatomical structures, namely the thalamus and the third ventricle, around the third ventricle based on the combination of anatomical knowledge and image analysis technique.

In contrast to conventional methods in which the third ventricle is segmented, the method embodying the present invention extracts the midlines of the third ventricle based on the local symmetry of the cerebrospinal fluid (the third ventricle) and the grey matter (the thalamus). The third ventricle plane is taken to be the least square fit plane of all the midlines of the third ventricle. The width of the third ventricle is calculated as the distance between two lines parallel to the third ventricle plane and tangential to the third ventricle on the axial slice containing the anterior and posterior commissures.

References:

1. Kim D.D. and Choi J.U., Huh R, Yun P. H., Kim D.I. – Quantitative Assessment of Cerebrospinal Fluid Hydrodynamics Using a Phase-Contrast Cine MR Image in Hydrocephalus. Childs Nerv the Syst 1999 Sep; 15 (9): 461-7.
2. Soininen H, Reinikainen K. J., Puranen M, Helkala E-L, Paljarvi L, Riekkinen P.J. – Wide 3rd Ventricle correlates with Low Choline acetyltransferase activity of the neocortex in Alzheimer patients – Alzheimer Dis. Assoc Disord 1993; 7: 39-47.
3. Beyer J. L., Krisnan K. R. – Volumetric Brain Imaging Findings in Mood Disorders – Bipolar Disord. 2002, Apr; 4(2): 89-104.
4. Ali S.O., Denicoff K.D., Altshuler L.L., Hauser P, Li X, Conrad A.J., Smith-Jackson E.E., Leverich G.S., Post R. M. – Relationship Between Prior Course of Illness and Neuroanatomic Structures in Bipolar Disorder – A Preliminary Study – Neuropsychiatry, Neuropsychol. Behav, Neurol 2001 Oct– Dec; 14 (4); 227-32.
5. Soininen H, Reinikainen K. J., Puranen M, Helkala E-L, Paljarvi L, Reikkinen P.J. – Wide Third Ventricle Correlates with Low Choline Acetyltransferase Activity of the Neocortex in Alzheimer patients – Alzheimer Dis. Assoc Disord 1993; 7: 39-47).

Claims:

1. A method for extracting third ventricle information from images of a plurality of axial slices of a third ventricle of a brain having an anterior commissure and a posterior commissure, the third ventricle having a third ventricle plane and a width, the method comprising:
 - (a) determining a third ventricle midline for each of a number of the axial slices;
 - (b) determining the orientation of each of the midlines;
 - (c) generating a histogram of the orientations of the midlines;
 - (d) determining the peak of the histogram to provide a peak orientation;
 - (e) selecting the midlines having an orientation within a predetermined angle from the peak orientation; and
 - (f) calculating the third ventricle plane from the midlines having an orientation within the predetermined angle from the peak orientation.
2. A method according to claim 1 wherein the step of calculating the third ventricle plane comprises calculating the least square fit plane of the midlines having an orientation within the predetermined angle from the peak orientation.
3. A method according to claim 2 wherein the step of calculating the third ventricle plane further comprises:
 - (i) calculating the maximum distance from the least square fit plane to the midlines having an orientation within the predetermined angle from the peak orientation,
 - (ii) generating a histogram of the maximum distance of the midlines having an orientation within the predetermined angle from the peak orientation to the least square fit plane,

- (iii) determining the peak of the histogram of the maximum distance of the midlines to the least square fit plane,
 - (iv) selecting the midlines lying within a predetermined distance of the peak, and
 - (v) recalculating the least square fit plane using the selected midlines to generate the third ventricle plane.
4. A method according to any one of the preceding claims, further comprising calculating the width of the third ventricle.
 5. A method according to claim 4, wherein the step of calculating the width of the third ventricle comprises determining the axial slice having the anterior commissure and the posterior commissure, determining two lines parallel to the third ventricle plane in said determined slice, said two lines being tangential to the image of the third ventricle in said slice to indicate the boundary between the third ventricle and grey matter, and calculating the distance between the two parallel lines, said distance being representative of the width of the third ventricle.
 6. A method according to any one of the preceding claims, wherein the step of determining the third ventricle midline for each of a number of the axial slice s_i comprises calculating the local symmetry index of a searching line segment, the third ventricle midline being the searching line segment that has the minimum local symmetry index.
 7. A method according to claim 6, wherein the local symmetry index $lsi(x,y,s_i, \theta)$ is calculated according to the following:

$$|ls(x,y,s_i,\theta)| \times lsi(x,y,s_i,\theta) = \sum_{(x_s, y_s)} \sum_k DifG(x_s, y_s, s_i, k)$$

where:

$|ls(x,y,s_i,\theta)|$ is the length of the searching line segment,

$ls(x,y,s_i,\theta)$ is the searching line segment of voxel (x,y,s_i) with the searching angle θ , and (x,y,s_i) the searching point,

$\cos(90^\circ + \theta)$ is denoted as $c90\theta$,

$\sin(90^\circ + \theta)$ is denoted as $s90\theta$,

$\text{fabs}(g(x_s + k \times c90\theta, y_s + k \times s90\theta, s_i) - g(x_s - k \times c90\theta, y_s - k \times s90\theta, s_i))$ is denoted as $\text{DifG}(x_s, y_s, s_i, k)$, where fabs is the absolute value function, the contribution of voxel (x_s, y_s, s_i) to $lsi(x, y, s_i, \theta)$ being:

$\text{DifG}(x_s, y_s, s_i, k1) + \text{DifG}(x_s, y_s, s_i, k2) + \text{DifG}(x_s, y_s, s_i, k3) + \text{DifG}(x_s, y_s, s_i, k4) + \text{DifG}(x_s, y_s, s_i, k5)$, $k1, k2, k3, k4$, and $k5$ are constants.

8. A method according to claim 7, wherein $k1$ is around 0.5mm.

9. A method according to claim 7, wherein $k2$ is around 1mm.

10. A method according to claim 7, wherein $k3$ is around 3mm.

11. A method according to claim 7, wherein $k4$ is around 5mm.

12. A method according to claim 7, wherein $k5$ is around 7mm.

13. A method according to claim 5, wherein the step of determining the axial slice having the anterior commissure and the posterior commissure comprises:

- (1) calculating the x co-ordinate of the voxel x_i for all of the axial slices where the third ventricle is present such that this voxel's y co-ordinate is the mass centre of s, y_c , and (x_i, y_c, s_i) is on the third

ventricle plane, that is $x_i = -(d + c s_i + b y_c)/a$, where (a, b, c) is a unit normal vector and d is a non-positive constant;

(2) generating the searching line segment from (x_i, y_c, s_i) such that the line segment is on the third ventricle plane and its centre is (x_i, y_c, s_i) ;

(3) calculating the average grey level avg_i of the searching line segment;

(4) comparing the average grey level avg_i for different axial slices s_i and determining the axial slice having the anterior commissure and the posterior commissure.

14. A method according to claim 13 wherein the step of determining the axial slice having the anterior commissure and the posterior commissure comprises for T1-, PD-weighted, FLAIR, and SPGR MR datasets, determining the axial slice with minimum average grey level avg_i .

15. A method according to claim 13 wherein the step of determining the axial slice having the anterior commissure and the posterior commissure comprises for T2-weighted MR datasets comprises determining the axial slice with maximum average grey level avg_i .

16. An apparatus arranged to perform a method for extracting third ventricle information from images according to any one of the preceding claims.

17. A computer program product comprising computer program instructions readable by a computer apparatus to cause the computer apparatus to perform a method according to any one of claims 1 to 15.

**ABSTRACT****Method And Apparatus For Extracting Third Ventricle Information**

A method for extracting third ventricle information from images of a plurality of axial slices of a third ventricle of a brain comprises determining a midline for each of a number of the axial slices, determining the orientation of each of the midlines, generating a histogram of the orientations of the midlines, determining the peak of the histogram to provide a peak orientation, selecting the midlines having an orientation within a predetermined angle from the peak orientation and calculating the third ventricle plane from the midlines having an orientation within the predetermined angle from the peak orientation.

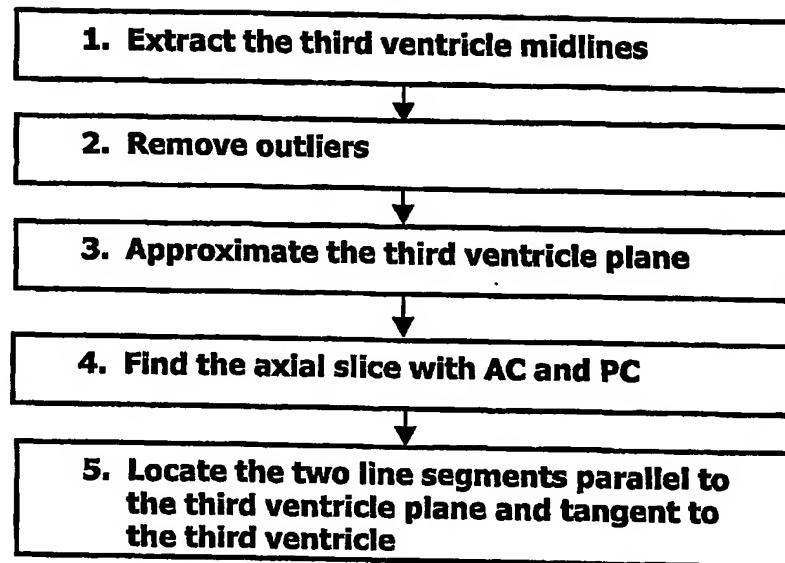
Figure 1

SECRET
G00002

1/1

100100
01631624

Figure 1



**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☒ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.